JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

# Formulation and evaluation of Silymarin loaded Matrix Tablets using Karaya gum

**Khushboo lavania[1*], Avdhesh Sharma[2]**

1. B.S.A.College of Pharmacy, Mathura ( U.P)
2. Advanced Medtech Solutions, Vadodara, India

## ABSTRACT

The major objective of the present work is to formulate and characterize Silymarin-loaded matrix tablets using Karaya Gum Powder as a release-controlling polymer. The matrix tablets were prepared by using the wet granulation method and characterized for their quality control attributes including hardness, weight variation, friability, and content uniformity. Further, matrix tablets were also characterized for their in-vitro release in phosphate buffer pH 6.8 using the Paddle type dissolution apparatus. The release kinetics models were applied to the dissolution data to predict the mechanism of release. The effect of increasing the concentration of Karaya gum on the release rate was studied. All the prepared batches of matrix tablets containing Silymarin have shown good quality control attributes and passed the requirements. The release rate of Silymarin was found to be decreased with increasing the concentration of Karaya gum in matrix tablets. The release kinetic model indicated the zero-order release for the matrix tablets prepared with Silymarin and Karaya gum in a ratio of 1:1.25. The storage stability of the optimized batch of matrix tablets was also carried out up to 60 days under 40°C and 75% RH. The result showed no color change and no significant difference in the percentage of drug release. Hence, the optimized batch of matrix tablets was found to be stable.

**KEYWORDS:** Silymarin, Karaya Gum, Matrix Tablet, Zero-order, Hepatoprotective,

## INTRODUCTION

The goal of a sustained release (SR) indefinite quantity kind is to keep up therapeutic blood or tissue level of the drug for associate extended amount. This is often typically accomplished by making an attempt to get zero order unleash from the indefinite quantity from[1]. The term “Controlled release” includes that means that goes on the far side the scope of sustained drug action. It conjointly implies the foregone conclusion and duplicability within the drug unleash dynamics which implies that {the unleash|the discharge} of drug ingredients from a controlled release drug delivery system yield at a rate profile that's not solely certain kinetically, however conjointly

duplicatable from one unit to another[2]. Within the gift investigation, studies were below taken to formulate and measure oral controlled unleash drug delivery system (CRDDS) of silymarin wide employed in the treatment of Hepatoprotective, Hepato-regenerative and Anti-hepatotoxic. it's freely soluble in wood spirit. It's elimination half-life of roughly half dozen hours3. supported these physico-chemical and bio-pharmaceutical properties, silymarin was chosen as a drug candidate for developing metallic element pill formulation. so as to boost the absorption and its oral bioavailability, we've got tried to formulate a controlled drug delivery system mistreatment silymarin with HPMC K4M as drug and compound severally.

Traditional medicinal plants have been important from ancient times (before 2500 B.C). People are wishing on plants in either prophylactic or the therapeutic arsenal to revive and maintain health. Important sources of many of the biologically active compounds are plants. According to ayurveda that part of seeds of milk thistle contains several active compounds like flavonoids, terpenoids, alkaloids, polyphenols, tannins, and saponins. It is blessed with hepatoprotective, anti-hepatitis B, anti-lithic, anti-HIV and anti-hypertensive. Hepatic disorders have far reaching consequence, given the critical dependence of other organs on the metabolic functions of the liver.

**Sylimarin**

Silymarin a flavonolignan from 'milk thistle' (Silybummarianum) is employed within the treatment of liver diseases. The half-life of Silymarin is about 4- 6 hrs. Since it has a very low bioavailability of 20%-50% and poor water solubility multiple doses are needed to maintain a constant plasma concentration for a good therapeutic response and improved patient compliance. It is a mixture of mainly three flavonolignans like silybin A and B, silidianin and silichristin with silybin being the most active. Silymarin has been used medicinally to treat liver disorders including acute and chronic viral hepatitis, toxin/ drug-induced hepatitis, cirrhosis, enhancing the activity of cell membrane and alcoholic liver diseases. It has also been reported to be an effective in certain cancers.

*Silymarin (Silybummarianum)* has been used since ancient times as a liver tonic. The English herb doctor and medico Nicolas Culpepper (1616–1654) noted that milk thistle are often accustomed open the obstructions of the liver and spleen and thereby is sweet against the jaundice and its use in liver disease. Sylimarin is reported to have effects as hepatoprotective effect, Antioxidant effect, Anti-inflammatory effects, Anti-tumour effect, Antidiabetes effect, Inhibition the production of Nitrous oxide, decrease the activity of phospholipase and Protection of the cell membrane.

The Purpose for this study was to develop the silymarin matrix tablets by the direct compression technique and their invitro analysis.

**Materials**

*Silymarin*was obtained from micro laboratories ltd, (Hosur, India). Sterculia gum as a present sample received from Nutriroma Company, Hyderabad. The Polyethylcellulose, starch, and talc and magnesium stearate was purchased from S.D. Fine chemicals, Mumbai, all alternative solvents used were of analytical grade.

**Methods**

**Preparation of Silymarin matrix tablets**

Matrix tablets each containing 400mg of Silymarin were prepared by Wet- Granulation method using sterculia gum. The tablets prepared were as per the formulae given in Table 1. Silymarin, Diluents (lactose) and polymer (sterculia gum powder) in various ratios like 0.25%, 0.5%, 1.1%, 1.5% and 2% were taken accurately and blended thoroughly. The blend was moistened with the distilled water to get damp mass. The damp mass was then passed through sieve no 12 and the granular mass obtained was dried in a hot air oven at $60^{O}$C for 1hr. The dried granules were passed through sieve no 16 to get free-flowing and uniform sized granules. The granules were lubricated with 2% of talc and 2% of magnesium stearate were added which is previously passed through sieve no. 100. The resulting mixture was compressed by Cadmac 16 station tablet punching machine to a hardness of 7.5-8 kilogram/sq.cm using flat punches.

**Table 1: Formulation of Silymarin Matrix Tablet**

| **Ingredients** | **Formulation** | | | | |
|---|---|---|---|---|---|
| | **F1 (mg) D:P(1:0.25)** | **F2 (mg) D:P(1:0.5)** | **F3 (mg) D:P(1:0.75)** | **F4 (mg) D:P(1:1)** | **F5(mg) D:P(1:1.75)** |
| Silymarin | 140 | 140 | 140 | 140 | 140 |
| Sterculia gum | 35 | 70 | 105 | 140 | 175 |
| Lactose Monohydrate | 181 | 146 | 111 | 76 | 41 |
| Poly vinyl Pyrrolidone (PVP K 30 | 16 | 16 | 16 | 16 | 16 |
| Mg.Sterate | 12 | 12 | 12 | 12 | 12 |
| Sodium Lauryl Sulphate (SLS) | 16 | 16 | 16 | 16 | 16 |
| Total weight mg | 400 | 400 | 400 | 400 | 400 |

**Evaluation of tablets**

**Evaluation of pre- compression properties of granular bed of sylimarin matrix tablet.**

| Formulation | Angle of repose(θ) | | Bulk density ($g/cm^3$) | Tapped density ($g/cm^3$) | Compressibility index % | Hauser's ratio |
|---|---|---|---|---|---|---|
| | Before adding glidant | After adding glidant | | | | |
| F1 | 25.51±0.3 | 24.48±0.4 | 0.67±0.2 | 0.71±0.09 | 5.3±0.4 | 1.11±0.1 |
| F2 | 25.67±0.3 | 24.40±0.1 | 0.58±0.8 | 0.63±0.04 | 9.3±0.9 | 1.12±0.2 |
| F3 | 25.66±0.3 | 24.20±0.1 | 0.58±0.2 | 0.63±0.04 | 8.1±1.1 | 1.13±0.1 |
| F4 | 27.22±0.2 | 25.13±0.2 | 0.43±0.1 | 0.49±0.01 | 8.1±0.9 | 1.11±0.8 |
| F5 | 26.28±0.4 | 24.70±0.2 | 0.51±0.6 | 0.55±0.01 | 5.9±0.9 | 1.12±0.4 |

**Evaluation of post- compression properties of granular bed of sylimarin matrix tablet.**

| Formulation | Weight variation | Thickness | Diameter | Hardness | Friability % | Drug content % |
|---|---|---|---|---|---|---|
| | (mg) | (mm) | (mm) | ($kg/cm^3$) | | |
| F1 | 399±0.1 | 5.5±0.1 | 13.5±0.1 | 7.6±0.1 | 0.56 | 99.7±1.2 |
| F2 | 398±0.3 | 5.4±0.2 | 13.7±0.1 | 7.0±0.3 | 0.72 | 98.2±1.0 |
| F3 | 398±0.2 | 5.2±0.1 | 13.6±0.1 | 6.6±0.1 | 0.65 | 99.8±0.7 |
| F4 | 399±0.4 | 5.4±0.4 | 13.6±0.1 | 6.8±0.4 | 0.79 | 98.9±1.1 |
| F5 | 398±0.9 | 5.9±0.2 | 13.2±0.2 | 7.0±0.2 | 0.67 | 99.2±0.8 |

The developed tablets square measure evaluated for hardness (shah et al., 1997), friability, thickness, and weight variation (Subramanyam, 1998). Twenty tablets were taken and weighed individually. Average weight was calculated standard deviation and percent coefficient of variance was compared.for estimation of drug content (Subramanyam and Thimmasetty, 2002). Standard silymarin100 milligram was dissolved in 100ml methanol to make 1000µg/ml stock solution. From the above solution aliquots of 0.6 ml, 0.8 ml, 1 ml, 1.2 ml, 1.4 ml, 1.6 ml were taken in a separate 10 millilitre volumetric flasks then make up the volume with methanol. An amount of the powdered tablet and capsule equivalent to 100 milligram of silymarin was weighed accurately, and extracted into

3 × 20 ml portions of chloroform with shaking. The residue was filtered using Whatmann No. 42 filter paper. The filtrate was evaporated to dryness under vacuum and the remaining drug was dissolved in methanol and diluted to 100 millilitre. Stock solution of concentration of 1-10 µg/ml was prepared appropriately diluted with respective dissolution medium and the series of solutions were subjected to ultra-violet spectroscopy and recoded at 286 nm.

**In vitro dissolution study**

The pill samples were subjected to in-vitro dissolution studies mistreatment USP kind a pair of dissolution equipment at 37±2°C and fifty rate speed. As per the official recommendation of USFDA, 900 cubic centimeter of zero.1 N Hcl (2hrs) and pH scale half dozen.8 Phosphate buffer (next eighthrs) was used as dissolution medium. Aliquot adequate to five mil was withdrawn at specific time intervals and. The dissolution media volume was complemented with a recent and equal volume of blank media (0.1 N Hcl). The aliquots were filtered and scanned with acceptable dilution and quantity of silymarin discharged from the pill samples determined spectrophotometrically at a wavelength of 286 nm by examination with the quality standardization curve.

Stability study

Stability is made public as a result of the "capacity of the drug merchandise to remain within specifications established to substantiate its identity, strength, quality and purity". in several words, the soundness of a drug is its ability to resist deterioration. This stability was meted out on the optimized formulation. the soundness studies were performed at 450±20C and (75% ± ball RH) for sixty days. when Associate in Nursing interval of fifteenth, 30th, forty fifth and sixtieth days. The sample was withdrawn and pill analysis tests were conducted. There was no color modification and there was no deviation within the proportion of drug unharness conjointly. It showed that every one formulations stay stable for sixty days. , it's necessary that the patient receive the same dose of a drug throughout the complete of the shelf-life.

Results and Discussion

UV spectrophotometry

Absorption maxima of silymarin were detected at two hundred and eighty seven metric long measure and overlay spectra of concentration vary 6-16 (µg/millilitre) was recorded (Figure 1). Absorbance at totally wholly completely different concentration showed in (Table 2). spatial property graph was showed in (Figure 2). Optical characteristics data showed in (Table 3).

**Table 2: Calibration data for analysis of Silymarin at 287nm**

| Concentration (µg/ml) | Absorbance Mean ± S.D. |
|---|---|
| 6 | 0.247±0.003 |
| 8 | 0.326±0.002 |
| 10 | 0.398±0.002 |
| 12 | 0.483±0.001 |
| 14 | 0.559±0.001 |
| 16 | 0.634±0.001 |

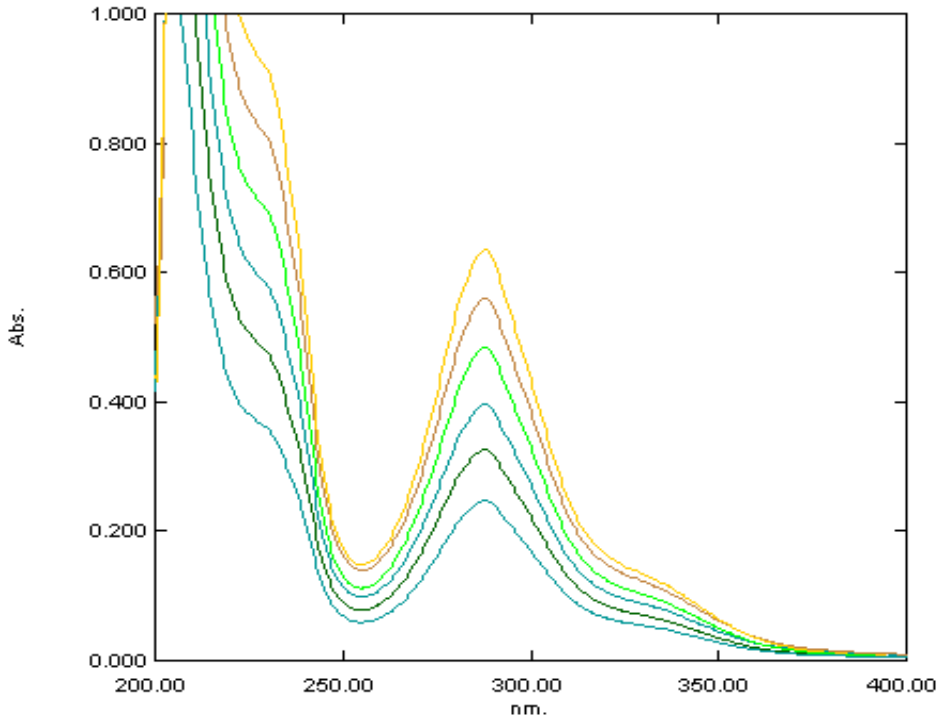


**Figure 1: Overlay spectrum of standard silymarin**

**Evaluation of blend and tablets**

The tablets of different formulations F1 to F5 were evaluated for various parameters hardness, diameter, thickness, friability, proportion weight variation, and percentage drug content.Before compression of the powder preformulation studies such as bulk density, angle of repose, tapped density, compressibility index, and Hausner's

ratio were determined for all formulations. The angle of repose and compressibility index ranged from 24.200 - 25.130 and 5.3 to 9.3 respectively.

The result of bulk density and tapped density were ranged from 0.43 to 0.67 and 0.49 to 0.71 respectively. The hardness of the tablets ranged from 6.6 to 7.6 respectively. The thickness and diameter of the tablets ranged from 5.2 to 5.5 and 13.2 to 13.7respectively. The in-vitro drug unleash information were fitted to four in style exponential equations (zero order, 1st order, higuchi, and koresmayerpeppas). The drug release of all the formulations was found to be followed zero order kinetics as correlation coefficient ($r^2$) values are higher than that of first order kinetics. By incorporating the release data in Higuchi and erosion models, the $r^2$ values of Higuchi model were found to be slightly greater than erosion model. So this means drug unleash from matrix tablets followed diffusion mechanism. To any make sure the precise mechanism of drug unleash the information was incorporated into koresmayer-peppas model and therefore the mechanism of drug unleash was indicated in step with the worth of release exponent(n) the release exponent value 'n' of F1-F5 were 0.28 to 0.78. So it indicates all the formulations F1 to F5 undergo non- fickian diffusion mechanism.The stability studies were performed at $45^0 \pm 2^0$C and (75% ± 5% RH) for sixty days. After an interval of $15^{th}$, $30^{th}$, $45^{th}$ and $60^{th}$days. The sample was withdrawn and tablet evaluation test were conducted. There was no colour change and there were no deviation in the percentage of drug release also. It showed that all formulations remain stable for sixty days.

**In vitro release studies**

From the in vitro drug release studies, the percentage drug release of all formulations after 10 hours using sterculia gum was found to be 86.78% (silymarin:karayagum)(1:0.25), 81.64%(1:0.5),73.92%(1:0.75). The results of the in-vitro release studies of all formulations are graphically represented as shown in fig.1.

In-vitro release of silymarin from the formulation without polymer was found to be 99.0% in 3.5 hours. When the polymer ratio increased, the percentage drug release of silymarin was deceased from controlled release dosage form.

**Release Kinetics of Silymarin Matrix Tablets**

| Formulations | Zero order | First order | Higuchi | Peppas (n) |
|---|---|---|---|---|
| **F1(1:0.25)** | 0.9944 | 0.8863 | 0.9076 | 0.9177 |
| **F2(1:0.5)** | 0.991 | 0.869 | 0.9142 | 0.9161 |
| **F3(1:0.75)** | 0.9878 | 0.89 | 0.9184 | 0.9146 |
| **F4(1:1)** | 0.9871 | 0.744 | 0.9199 | 0.94 |
| **F5(1:0.25)** | 0.9937 | 0.9517 | 0.921 | 0.9186 |

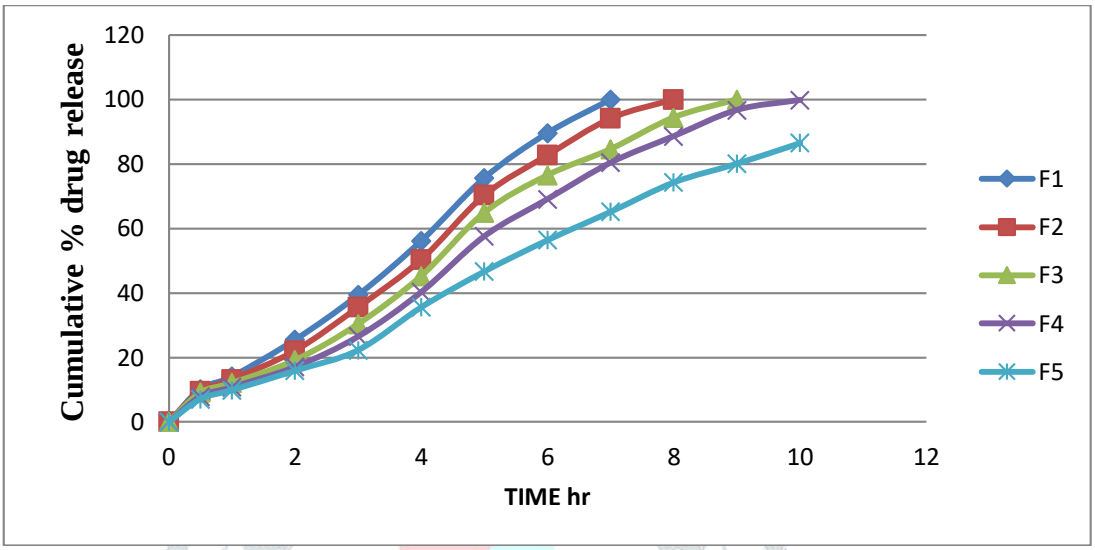


**Fig. 1: Zero Order Plot for F1, F2, F3, F4, F5**

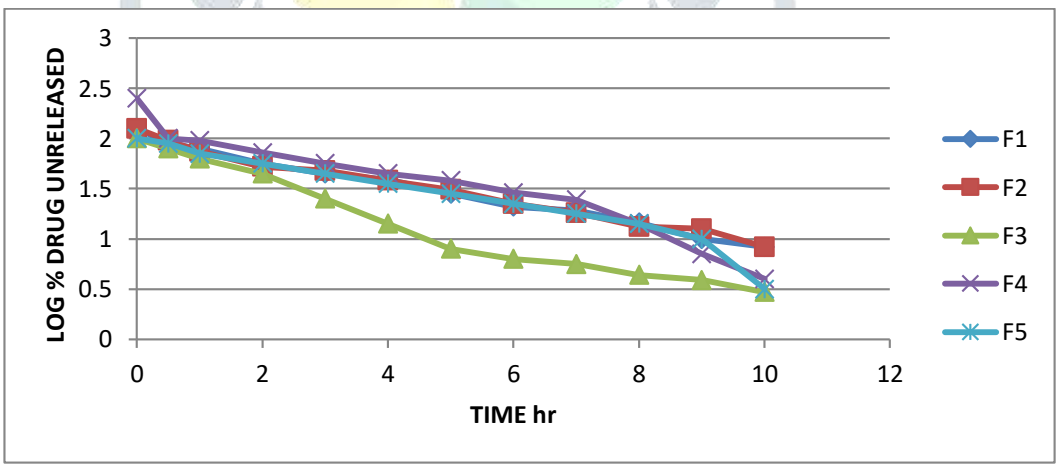


**Fig. 2: First Order Plot for F1, F2, F3, F4, F5**

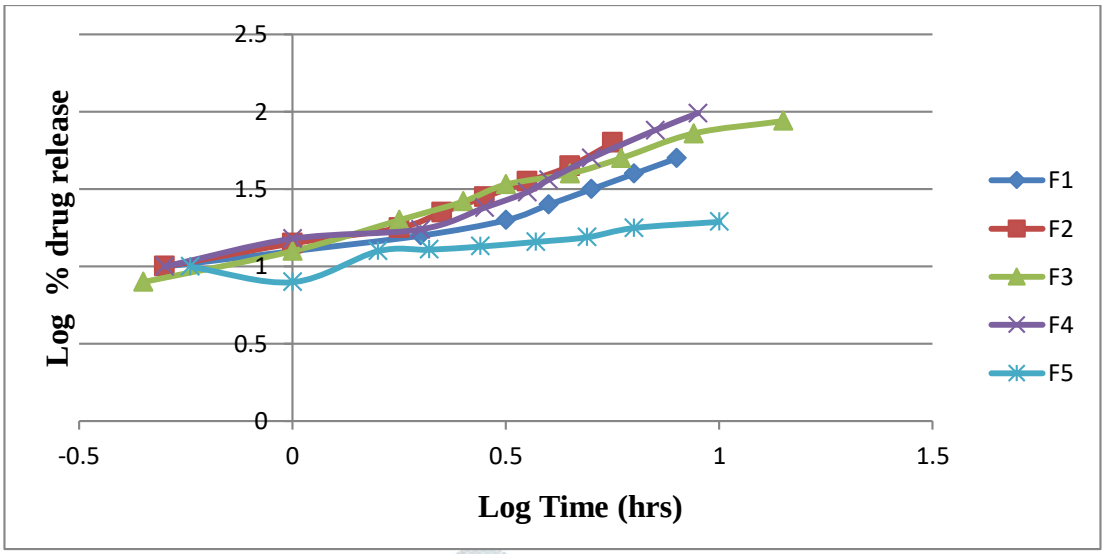


**Fig. 3: KoresmayerPeppas Plots F1, F2, F3, F4, F5**

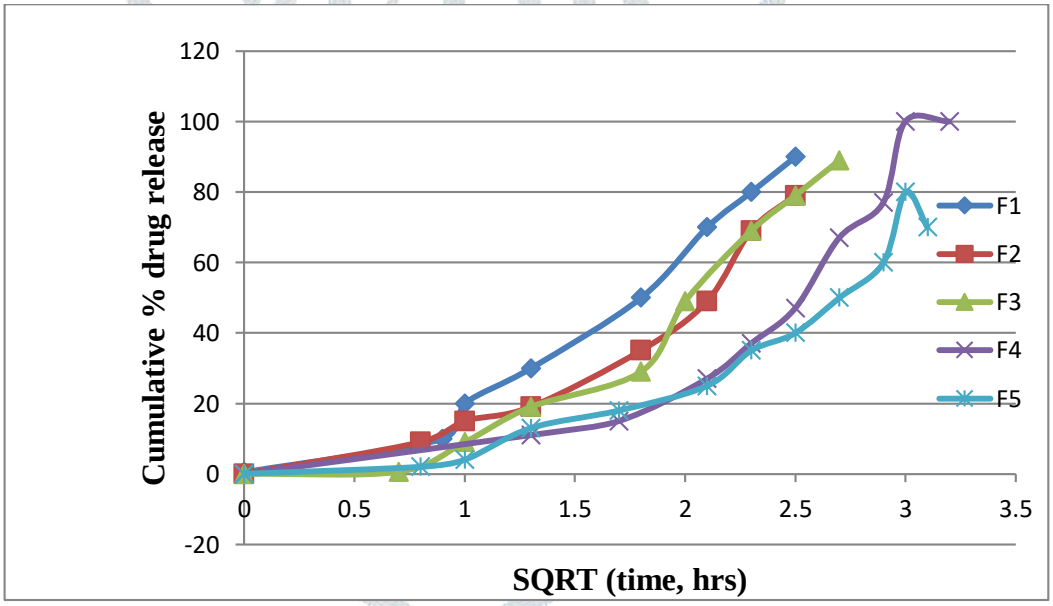


**Fig. 4: Higuchi Plot for F1, F2, F3, F4, F5**

## CONCLUSION

The present study was aimed at developing a matrix tablet of sylimarin it has the use swellable polymer, release retardant and an alkalizing agent which proved to be an ideal formulation, as it released the drug in a controlled manner for extended to the period of time. The study reveals that the release of drug, sylimarin exhibited diffusion coupled with erosion drug release mechanism, followed first- order kinetics. The optimized formulation

provides the simplest lead to F1 to F5 discharged minimum quantity of drug within the physiological surroundings of abdomen, intestine and sustained the drug upto 24 hours.

To carry the maximum amount of drug release more than 75% at the end of 12 hours.

It was found that an increase in the concentration of excipients in polymeric ratio decreases the drug release. Karaya gum is non-carcinogenic, biocompatible, and high drug holding capacity.

It can be concluded that among all the formulations F4 containing 1.5% of sterculia gum powder was found to release the drug in a slow controlled manner with maximum drug release of 99.8 percent and found to follow zero-order release kinetics with Non-Fickian diffusion mechanism.

**References**


1. Aulton ME and Wells TI “Pharmaceutics the science of dosage form design”, Churchill Livingstone, London, 1998, pp. 159-161.
2. Brirish Pharmacopoeia, BririshPharmacopoeialCommision, London, 2: A-209, A-299 (2000).
3. Ganesh S. Radhakrishnan, M. Ravi M. Prasannakumar D and Kalyanij, Invitro evaluation of the effect of combination of hydrophilic and hydrophobic polymers on controlled release zidovudine matrix tablets, Indian J Pharmaceutical Sciences.70: 461-465(1999).
4. Manekar NC, Gandhi SD and Joshi, Controlled Drug Delivery System, the Eastern Pharmacist, 43:41-45(1999).
5. Mutalik Srinivas and HiremathDoddayya, Formulation and evaluation of chitosan matrix tablets of nifedipine. The Eastern Pharmacist, 63:109-111(2000).
6. Reddy R.B.D.,MalleswariK and Narayan L.,Formulation and in- vitro evalution of sylimarin floating matrix tablets International journal of pharmacy and Pharmaceutical Sciences,45,2012 pp:45-56.
7. Subramanyam CVS and Thimmasetty T., Laboratory manual of physical pharmaceutics. VallabhPrakashan, Delhi,1st edition, pp.24,32 and 46-53(2002)

8. Sharma YR, Elementary Organic Spectroscopy Principles and chemical application, S.Chand and CO.New Delhi,pp 65-133 (2005)
9. Pharmacopoeia of India, Ministry of Health and Family Welfare, Govt.of India, Controller of Publication, New Delhi, 736(1996).
10. Vidyadhara S Rao, PR and Prasad Jha, Formulation and evaluation of Propranolol Hydrochloride and controlled release matrix tablets Indian J Pharmaceutical Sciences 66: 188-192 (2004).
11. Radjabian T,Rezazadeh S andHuseini F.H., Analysis of Silymarin components in the seed extracts of some milk thistle ecotypes from Iran by HPLC. Iranian Journal of Science & Technology, 32-(2008), pp 405-420.
12. Mallikarjuna G,Ramakrishna S.and Shanta K., Formulation and evaluation of Colon specific microbial degradable matrix tablet using sterculia gum as carrier. Journal of pharmacy and Pharmaceutical Sciences, 22(2009), pp.48-55.
13. SubrahmanayamCVS, Text book of physical pharmaceutics, vallabhprakashan, Delhi 1st edition pp.215-223(1998).
14. Shah D, Shah Y and Rampradhan M., Development and evaluation of controlled release diltiazem hydrochloride micro particles using cross- linked polyvinyl alcohol, Drug Dev. Pharm,23:567-574(1997).
15. Agarwal SP andKhanna Rajesh, Physical Pharmacy, 2nd edition, New Delhi. CBS Publishers and distributors, 2000; 247.
16. Vidyadhara S Rao, PR and Prasad JA. Formulation and evaluation of propranolol hydrochloride oral controlled release matrix tablets. Indian J.Pharm.Sci.66:182-192(2004).
17. Yeole PG, GalgatteBabla IB and Nakhat PD, Design and evaluation of xanthan gum based sustained release matrix tabletsof diclofenac sodium. Indian J.Pharm.Sci.68:185-189(2006).